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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/492,392	01/27/2000	Alain Commercon	03806.0464	9815

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FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
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EXAMINER	
LUKTON, DAVID	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 06/03/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/492,392	COMMERCON ET AL.	
	Examiner	Art Unit	
	David Lukton	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-28 and 30-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *28,30 and 31* is/are allowed.

6)☒ Claim(s) *17-27 and 32-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *22* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Pursuant to the directives of paper No. 21 (filed 3/21/03), claims 28, 32, 33 have been amended, and claim 29 cancelled. Claims 17-28, 30-35 remain pending.

Applicants' arguments filed 3/21/03 have been considered and found persuasive in part. The previously imposed §112, second paragraph rejections are withdrawn. In addition, the §112, first paragraph rejection of claims 28, 30, 31 is withdrawn. Claims 28, 30, 31 are now characterized as allowable.

*

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-27, 32-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As indicated previously, the factors for evaluating the need for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and

breadth of the claims. As indicated previously, the following references disclose either or both of the following: (a) compounds that failed to inhibit bacteria and (b) that compounds which failed to inhibit bacteria were minor structural variants of compounds that do inhibit bacteria: `

- Gavini ("Pyridazine N-oxides. III. Synthesis and in vitro antimicrobial properties of N-oxide derivatives based on tricyclic indeno[2,1- c]pyridazine and benzo[f]cinnoline systems", *Archiv der Pharmazie* **333** (10) 341-6, 2000) discloses the preparation and testing of a series of pyridazine N-oxides. With the exception of compounds 3a, 3b, 4b and 5b, the compounds "demonstrated no activity against bacteria" (page 342, col 2).

- Fudou ("Haliangicin, a novel antifungal metabolite produced by a marine myxobacterium. 1. Fermentation and biological characteristics", *Journal of Antibiotics* **54** (2) 149-52, 2001) discloses the isolation of haliangicin which is produced by a marine bacteria; the compound contains a conjugated tatraene moiety and exhibited no antibacterial activity.

- Juvvadi ("Structure-activity studies of normal and retro pig cecropin-melittin hybrids", *Journal of Peptide Research* **53** (3) 244-51, 1999) discloses the preparation and antibacterial activity of cecropin-melittin hybrid peptides. Also disclosed is that the "retro" analogs (the polarity of the amide bond reversed) lost antibacterial activity.

- Avrahami (*Biochemistry* **40** (42) 12591-603, 2001) studied the effects of amino acid substitutions on the antimicrobial activity of amphipathic antimicrobial peptides. Many of the compounds prepared lost antibacterial activity as a result of a single amino acid substitution. Although after-the-fact rationalizations were provided, the observed structure/ activity relationships could not have been predicted *a priori*.

In response to the foregoing, it is argued (response filed 3/21/03) that in imposing an enablement rejection, the examiner bears the burden of establishing doubt that the claimed

invention can be used in accordance with assertions in the specification. It is further argued (response filed 3/21/03) that the examiner has not met this burden. It is also argued that the specification makes various assertions about routes of administration, and dosages at which antibacterial activity might be achieved. It is also argued that the specification asserts that the claimed compounds undergo biodegradation at a slower rate than prior art Group A streptogramins. No results on biotransformation rates are disclosed, but whatever the susceptibility of the claimed compounds to monooxygenases, proteases, and other degradative enzymes, the question of antibacterial efficacy remains. It is also asserted in the specification that the claimed compounds are not toxic when adminstered at a dose above 300 mg/kg. While this may be true, it does not follow therefrom that the claimed compounds will exibit antibacterial activity. In addition, reference is made to Barriere (*Cur Pharm Design* **4**, 155, 1998), which discloses that streptogramin compounds which are patentably distinct from any of those claimed exhibit antibacterial activity. However, there is no evidence in Barriere that any of the claimed compounds exhibit antibacterial activity. Next it is argued (response filed 3/21/03) that if the examiner chooses to argue that utility for the claimed invention is lacking, he should provide evidence of such. However, as indicated in each of the previous Office actions, no rejection for lack of utility has been imposed.

Next, a comment is made (response filed 3/21/03) with respect to some of the references

cited by the examiner, i.e., Gavini, Fudou, Juvvadi and Avrahami. The argument is twofold: (a) that none of the references specifically concerns the claimed subject matter, and (b) the references do not sufficiently refute the statements of the specification. Each of the references does provide evidence that has direct bearing on the broader question of whether or not a skilled microbiologist would have been able to determine the antibacterial activity of a compound merely by viewing its structure. The cited references (Gavini, Fudou, Juvvadi and Avrahami) do support the conclusion that in endeavoring to achieve antibacterial activity, the structural elements that are necessary to achieve that objective cannot be predetermined in advance of experimentation, merely by considering the structure of a compound. There is no suggestion in the application as filed that a skilled microbiologist would have been able to determine, in advance of experimentation, which of the compounds disclosed in the references (Gavini, Fudou, Juvvadi and Avrahami) would more likely than not have exhibited antibacterial activity. Certainly for the compounds disclosed in the references, structure/activity relationships are "unpredictable". One would therefore expect such unpredictability (with respect to antibacterial activity) to be a feature of the present claims. Accordingly, for a streptogramin which has been shown by another microbiologist to exhibit antibacterial activity, and the structure subsequently modified, one cannot "predict", on the basis of any teaching in the instant application, whether such modification will lead to an increase in activity, an elimination

of activity or perhaps no change in activity. In the response filed 3/21/03, it is argued that the references fail to provide "specific technical support" for doubting the "exhaustive teachings" of the specification. However, the only teaching that is directly at issue is whether the claimed compounds exhibit antibacterial activity. The references cited by the examiner support the conclusion that where antibacterial activity is concerned, one cannot determine such activity merely by viewing a structure of a compound. Taken in conjunction with the the state of the art, and the absence of working examples, it is concluded that "undue experimentation" would be required to determine which of the compounds which exhibit antibacterial activity, and under what circumstances.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED AND ANY EXTENSION FEE PURSUANT TO 37 CFR 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 703-308-3213. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at (703) 308-2923. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

D. Lukton 5/27/03

CHRISTOPHER S. F. LOW
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